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| 09/678,016 | 10/02/2000 | Keith P. Wilson | VPI/96-03 DIV2 | 7947 |

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EXAMINER

ALLEN, MARIANNE P

ART UNIT PAPER NUMBER

1631

DATE MAILED: 11/20/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/678,016

Applicant(s)

WILSON ET AL.

Examiner

Marianne P. Allen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 August 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 23 and 27-36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 23 and 27-36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 18 March 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

Applicant's arguments filed 8/28/02 have been fully considered but they are not persuasive and/or are moot in view of the new ground(s) of rejection.

Claims 23 and 27-36 are under consideration by the examiner.

The rejection of the claims under 35 USC§ 101 as being non-statutory is withdrawn in view of applicant's amendments to the claims. The rejection of the claims under 35 USC § 101/112 as lacking utility (and therefore enablement) is withdrawn in view of the claims issued in parent application 08/640,164 (now U.S. Patent No. 6,128,582) and the fact that identification of chemical entities that associate with IMPDH (such as inhibitors) would be of interest to those of ordinary skill in the art. (See for example Saunders et al. (U.S. Patent No. 5,932,600).)

Claim Rejections - 35 USC § 112

Claims 23 and 27-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an enablement rejection.

Claim 23 is directed to a method for evaluating the ability of a chemical entity to associate with all or any part of a binding pocket defined by given structure coordinates. The steps set forth are to perform a fitting operation between the chemical entity and a binding pocket, analyzing the results to quantify the association, and outputting the quantification of association to a suitable output hardware. Independent claim 29 is similarly structured. It is noted that while the preamble of the claims identifies coordinates for the binding pocket, the step in the body of the claim does not. Note further that the body of the claim recites "a" binding

pocket implying more than one and not necessarily the one of the preamble. Thus, the body of the claims does not clearly specify the structure of the binding pocket that the chemical entity is being fitted to.

Secondly, the claims do not indicate that the **structure coordinates** of the chemical entity are used in the fitting operation. For example, page 14, lines 29-31, discusses loading the structures to be compared and defining the atom equivalences in these structures; however, the claims are not so limited. There is no guidance on other fitting operations for chemical entities that do not use such structural information.

Thirdly, the specification defines “associating with” as referring to a condition of proximity between a chemical entity or compound which can be covalent or non-covalent. (See at least page 13, paragraph bridging pages 27-28, and first full paragraph on page 28.) However, the steps of the claims do not have any limitations as to the determining these types of associations with the named amino acid positions and do not appear to require these proximities. The meets and bounds of a “fitting operation” do not appear to be defined in the specification. Applicant is requested to point to the portion of the specification that clarifies what is intended to be encompassed. In the absence of a clear definition, the type of quantification of the results of such an operation is not defined. It is not known from the specification in a general way what type of value the claims require (e.g. estimated interaction energy, conformation energy, etc.) nor what values constitute an association versus a non-association. The specification provides no examples using the structural coordinates of Figure 1 in the method as claimed. No fitting operation is performed for any chemical entity, no analysis of the results leading to

quantification of the association is performed, no output of this quantification is exemplified for the IMPDH binding pocket using any computational means.

Note that the claims are not limited to the programs set forth on pages 28-30 and 34 nor does the specification disclose the particular computational values these programs would generate that are considered to be limitations of the claims. The specification provides no guidance as to other fitting operations and analysis of the results of such fitting operations to quantify an association. It is unclear if visual inspection of a three-dimensional structure of a chemical entity in a docking program with the binding site (the only “output to a suitable output hardware” identified by the examiner in the specification) meets the limitation of quantifying the association.

Furthermore, while the preamble is directed to evaluating the ability of the chemical entity to association, there is no evaluation step or cut-off to determine whether or not the chemical entity is considered to associate.

While the specification appears to be directed to designing new compounds or identifying known compounds whose structural coordinates can be positioned within the structural coordinates of the disclosed binding pocket using known computational techniques (such as docking and *de novo* ligand design), the claims as written do not set forth this concept. Applicant is cautioned against introducing new matter into the claims.

Claims 28, 31, 34, 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 28 is confusing in its dependency upon claim 27. This claim requires fewer structural coordinates than claim 27. That is, it fails to contain all of the limitations of the claim upon which it depends. Claims 31 and 34 are likewise confusing in their dependency upon claims 30 and 33, respectively.

Claim 35 is confusing in failing to further define the binding pocket of claim 29 clearly. Note that the limitations of this claim refer to the molecule or molecular complex of the preamble which is not required by the body of the claim. If the claim was intended to require additional structural coordinates to define the binding pocket referred to in the body of the claim, this should be made clear.

Claim 36 is confusing in reciting "wherein said molecule or molecular complex comprises." As three components are listed it appears that only the complex was intended. Alternatively, the claim might be considered to mean any of 1-514 of IMPDH, XMP, or MPA which is confusing as the coordinates in Figure 1 are for the complex of IMPDH, XMP, and MPA (see page 8). In any event, claim 32 (upon which claim 36 depends) defines the binding pocket coordinates and it is unclear how this claim modifies these coordinates or the method claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 23 and 27-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bohm.

Bohm teaches the computer program LUDI for design of enzyme inhibitors by positioning small molecules (the instant chemical entity) into clefts of protein structures (the instant binding pocket), using particular calculations for fragment fitting to interaction sites (the instant fitting operation and analysis of the results to quantify the association) and outputting the three dimensional representation of the designed molecule in association with the enzyme used as input (which is considered to meet the requirement of step (c) as the resulting molecule is based upon the program calculations). Input for the program is three dimensional structure information.

Claim 23 is directed to a method for evaluating the ability of a chemical entity to associate with all or any part of a binding pocket defined by given structure coordinates. The steps set forth are to perform a fitting operation between the chemical entity and a binding pocket, analyzing the results to quantify the association, and outputting the quantification of association to a suitable output hardware. Independent claim 29 is similarly structured. The recited structural coordinates are considered to be nonfunctional descriptive material as it functions as input to the computer means. As the recited steps of the method are met by Bohm, each of the claims is obvious over this known method. How the program of Bohm functions is not altered by the input.

Applicant is reminded that MPEP 2106 states:

If the difference between the prior art and the claimed invention is limited to descriptive material stored on or employed by a machine, Office personnel must determine whether the descriptive material is functional descriptive material or nonfunctional descriptive material, as described supra in paragraphs IV.B.1(a) and IV. B.1(b). Functional

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descriptive material is a limitation in the claim and must be considered and addressed in assessing patentability under 35 U.S.C. 103. Thus, a rejection of the claim as a whole under 35 U.S.C. 103 is inappropriate unless the functional descriptive material would have been suggested by the prior art. In re Dembiczak, 175 F.3d 994, 1000, 50 USPQ2d 1614, 1618 (Fed. Cir. 1999). Nonfunctional descriptive material cannot render nonobvious an invention that would have otherwise been obvious. Cf. In re Gulack, 703 F.2d 1381, 1385, 217 USPQ 401, 404 (Fed. Cir. 1983) (when descriptive material is not functionally related to the substrate, the descriptive material will not distinguish the invention from the prior art in terms of patentability).

Common situations involving nonfunctional descriptive material are:

- a computer-readable storage medium that differs from the prior art solely with respect to nonfunctional descriptive material, such as music or a literary work,
- a computer that differs from the prior art solely with respect to nonfunctional descriptive material that cannot alter how the machine functions (i.e., the descriptive material does not reconfigure the computer), or
- a process that differs from the prior art only with respect to nonfunctional descriptive material that cannot alter how the process steps are to be performed to achieve the utility of the encoded on the medium, invention.

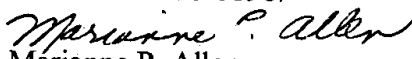
Conclusion

No claim is allowed.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is 703-308-0666. The examiner can normally be reached on Monday-Friday, 8:30 am - 2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 703-308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


Marianne P. Allen
Primary Examiner
Art Unit 1631

mpa
November 14, 2002


John J. Doll, Director
Technology Center 1600